Response to Low Shear Modeled Microgravity Indicates Translation of Lactobacillus acidophilus ATCC 4356 Benefits to Spaceflight

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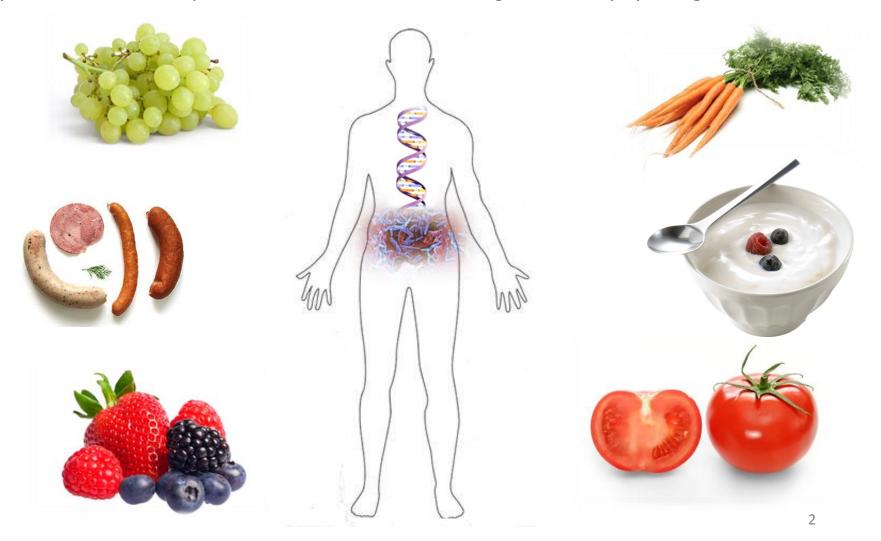


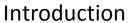


Food and Microbes: A Major Factor in Human State

Diet provides abundance of <u>naturally acquired microflora</u>

Symbiotic relationship with human contributes to digestive and physiological homeostasis





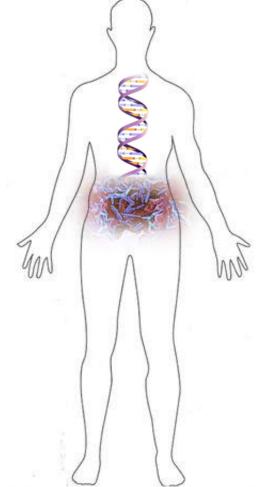


Food and Microbes: A Major Factor in Human State

In spaceflight, diet becomes "sterile"





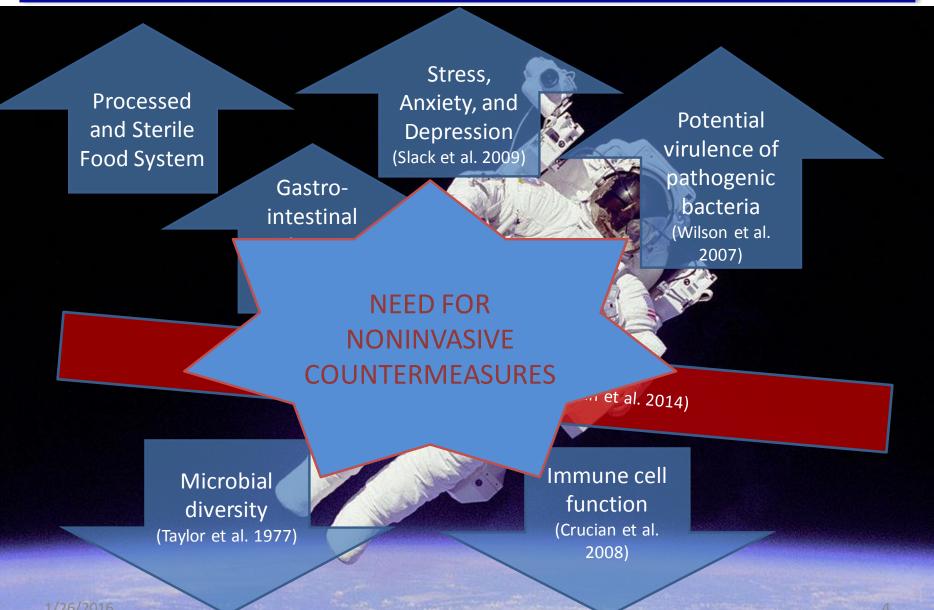






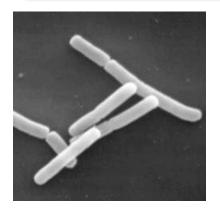


Human State in Spaceflight





Probiotics as a countermeasure



Generally Recognized as Safe Documented health outcomes

Lactobacillus acidophilus ATCC 4356

Reduce cold and flu like symptoms (Leyer 2009)

Reduce antibiotic associated diarrhea (Sazawal 2006)

Can deliver in spaceflight food system (Douglas 2014)

*Response to spaceflight or spaceflight analog environment has not been previously investigated



Low Shear Modeled Microgravity



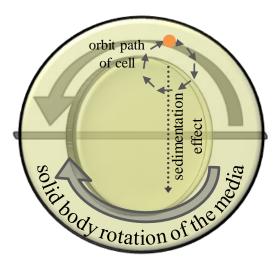
Rotating-wall vessel (RWV) Synthecon (Houston, TX)



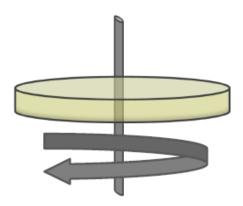


http://library.med.utah.edu/WebPath/GIHTML/GI162.html





Control Orientation





Objectives AND Methods

Determine the effect of LSMMG on

L. acidophilus ATCC 4356

Growth



Stress Response SURVIVAL THROUGH DIGESTIVE TRACT

pH 2, pepsin pH 8, pancreatic juice





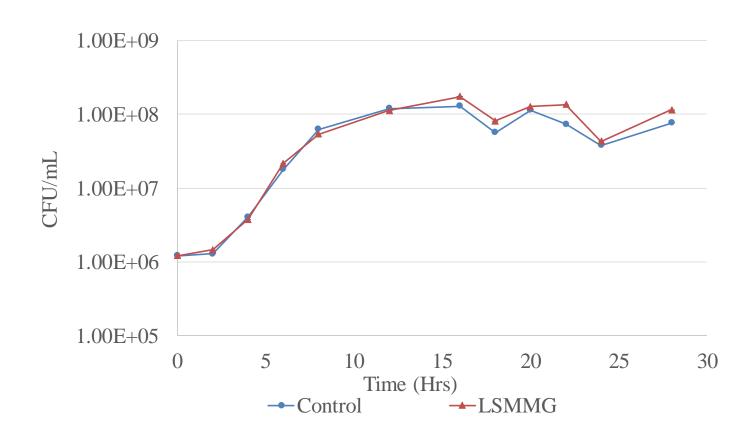
Transcriptome



Illumina MiSeq



Growth



1/26/2016

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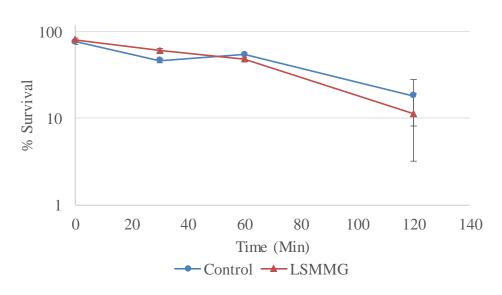


Stress Response

Simulated Gastric Juice



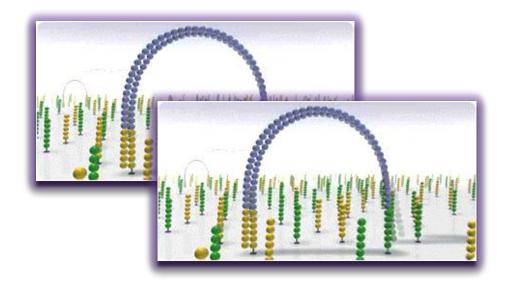
Simulated Small Intestinal Juice





Transcriptomic Response

UNALTERED GENE EXPRESSION



Study is a first for LSMMG gene expression in two areas...

Organism	Stress Response	Transcriptional Response	Pathogenicity Mechanism in the Intestine	Method of Culture	Reference
L. acidophilus	Unaltered resistance to simulated gastric and intestinal juice	Unaltered gene expression	Probiotic with the ability to persist in or colonize the intestinal tract	Anaerobic chamber with incubation temperature	This work
Pathogenic Escherichia coli and adherent-invasive E. coli	Increased resistance to acid, osmotic, thermal, and oxidative stress	Differential gene expression	Pathogen with the ability to actively invade or adhere to the intestinal epithelium	Ambient air within a microbiological incubator	Allen 2008 Chopra 2006
Salmonella enterica serovar Typhimurium	Increased resistance to acid, thermal, and osmotic stress	Differential gene expression	Pathogen with the ability to actively invade the intestinal epithelium	Ambient air within a microbiological incubator	Nickerson 2000 Wilson 2002, 2007
Enterobacter cloacae	Decreased resistance to acid and oxidative stress	Differential gene expression	Opportunistic Pathogen with the ability to invade intestinal epithelium	Ambient air within a microbiological incubator	Soni 2014



Conclusions

- The data suggests that there may be differences in the reaction of beneficial microbes to the low-fluid-shear of spaceflight compared to pathogens and that oxygen may be a component.
- The similar trends observed in the growth, survival through stress challenge, and gene expression between LSMMG and control grown L. acidophilus suggest that the strain will behave similarly in spaceflight and may be expected to confer Earth-based benefits.
- It is suggested that the introduction of GRAS probiotic microbes into the spaceflight food system has the potential for use as a safe, non-invasive, daily countermeasure for crew immune dysfunction.



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